REDESIGN OF WATER NETWORKS FOR EFFICIENT BIOCATALYSIS

Per-Olof Syrén, KTH Royal Institute of Technology, Sweden
per-olof.syren@biotech.kth.se

Key Words: Enzyme design, water, entropy, protein dynamics, biocatalysis.

The state-of-the art in the biocatalytic generation of renewable polymers, fine chemicals and medicines lays in enzyme discovery and engineering programs to afford enzymes with extended catalytic versatilities and enhanced performance [1]. However, the fundamental question how enzymes work, which has continuously fascinated researchers for almost 140 years, remains partly unsolved. We do not today fully understand the impact of enzyme motion and dynamics in driving biocatalysis, and the evolution of novel catalytic functions, which hampers the full potential of enzyme design. Herein, our fundamental understanding of how protein and solvent dynamics facilitates biocatalysis and the emergence of catalytic function is advanced through an interdisciplinary approach that merges computational enzyme design, bioinformatics, experimental biocatalysis and biophysics with state-of-the art protein mass spectrometry. We explore the untapped[2] opportunity to relocate water molecules in solvated binding pockets by protein design to afford biocatalysts with extended catalytic versatilities and improved properties (Figure 1). Based on an enhanced understanding of dynamics, recent results from our enzyme engineering and synthetic biology programs centered on expanding the catalytic scope of biocatalysts beyond nature's current capabilities for applications in textile recycling, material science and fine chemical synthesis will be high-lighted.

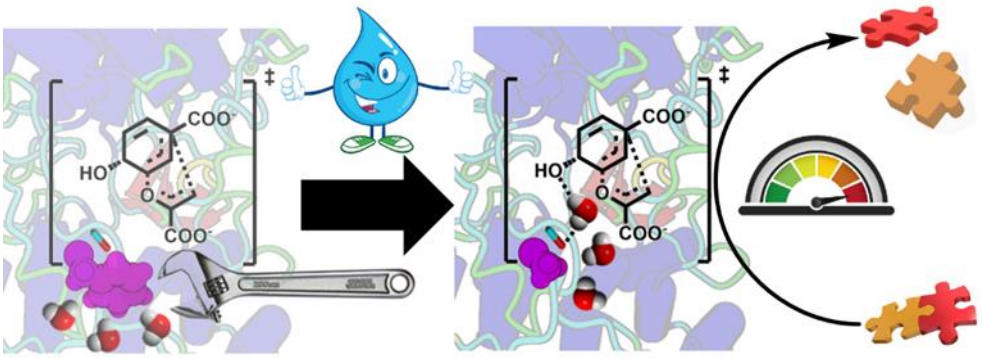

Figure 1 - Rewiring water networks in protein interiors impacts binding affinity, catalysis and the thermodynamic signature of biochemical processes through dynamic mechanisms, and thus has great potential to accelerate biocatalysis and provide new reaction mechanisms and chemistry, that were not yet explored in nature.

[1] H. Renata, Z. J. Wang and F. H. Arnold. Expanding the Enzyme Universe: Accessing Non-Natural Reactions by Mechanism-Guided Directed Evolution. Angew. Chem., Int. Ed., 2015, 54, 3351-3367.
[2] M. J. Fink and P.-O. Syrén. Redesign of water networks for efficient biocatalysis. Curr. Opin. Chem. Biol. 2017, doi: 10.1016/j.cbpa.2017.02.013.